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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,358	09/23/2005	Maximilian Grassberger	PD/4-32802A	1234

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,358	GRASSBERGER ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner for this current application at the USPTO has changed. Examiner Jean-Louis can be reached at 570-271-3503.

Response to Amendment

This Office Action is in response to the amendment submitted on 04/28/08. Claims 1-9 are currently pending in the application, with claims 7-9 having being newly added. Accordingly, claims 1-9 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Applicant's argument with respect to the specification and table as evidence that Applicant was in possession of the invention has been fully considered. Given that Applicant delineated various ratios that are purported to be synergistic and data that support a synergistic efficacy, Examiner contends that sufficient disclosure was indeed provided. As a result, the rejection under 35 U.S.C. § 112, first paragraph is withdrawn.

Applicant's contention that retinoids operate through the same physiological mechanism and therefore one of ordinary skill would likely conclude that all retinoids would behave synergistically according to the ratios and dosage of Applicant has been fully considered and is found persuasive. Indeed, all retinoids operate through retinoid

receptors and in light of the dosage and ratios provided by applicant, one of ordinary skill would have found obvious that all retinoids would necessarily behave the same way. As a result, the rejection under 35 U.S.C. § 112, first paragraph is withdrawn.

Applicant's argument that the Examiner interpreted erroneously the method of treatment as encompassing prophylaxis and that such definition is too stringent has been fully considered but is non-persuasive. Claims are examined in light of the specification, and given that applicant explicitly states on pg. 5 of the specification that treatment includes prevention, namely prophylactic or curative treatment, indeed the claims as previously presented fail to provide information that would allow the skilled artisan to practice the instant invention. Additionally, while applicant has provided a Stedman's Medical broad definition of curative, applicant decided to be his/her own lexicographer. Thus, in view of applicant's definition, the claims were examined to include the prevention and prophylaxis treatment as well as non-curative treatments. Moreover, Applicant failed to show any working examples in which applicant prevented or cured allergic dermatitis or other conditions. In regards to the predictability of preventing or curing of eczema, psoriasis, acne, atopic dermatitis, skin aging, sun damage, etc... Applicant has also failed to demonstrate that the composition of claim 1 is able to arrest each and every known and unknown cause of dermatological diseases, and furthermore that the composition works in all of the patients populations affected by such conditions. Thus, the rejection of claim 3 under 35 U.S.C. § 112, first paragraph

was proper. However, in view of applicant's amendment of claim 3, the rejection is thereby withdrawn.

Applicant's argument with respect to Ormerod who only teaches topical formulations and not oral or systemic formulations has been fully considered but considered moot. The claims as previously presented did not recite a mode of administration which is now claimed in newly added claims 7 through 9. Indeed, Ormerod et al. teach topical formulations comprising 33-epi-chloro-33-desoxyascomycin that avoids appearance of the macrolide in the blood at significant level for the treatment of dermatological disorders. Ormerod et al. further teach that the macrolide can be administered topically with the aid of a permeation modulator (see pg. 1, lines 23-25, pg. 3, lines 3-7 and pg. 5, lines 14-17) or orally. Moreover, Examiner respectfully points out that the rejection was rendered obvious in view of Hardman et al. who clearly disclose the use of retinoids with antibacterial agents in treating various dermatological conditions including acne. While Hardman et al. does not teach the combination of the macrolide with a retinoid, it is well within the purview of the skilled artisan to combine the two compositions of Ormerod and Hardman for the treatment of dermatological conditions as they both teach their individual compositions as useful for dermatological conditions. Moreover, as a general principle it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining them flows logically from their having been individually taught in the prior art. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06.**

If in fact, applicant contends that the prior art does not render obvious applicant's invention, Applicant is invited to present such unexpected results that render the prior art combinations non-obvious.

For the foregoing reasons, the rejection of claims 1-6 under 103 (a) remain proper. However, in view of applicant's amendment, the following modified 103 (a) Non-Final rejections are being made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-7, and 9 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Ormerod et al. (WO 99/24036, previously submitted by applicant) in view of Hardman et al. (Goodman & Gilman's: The Pharmacological Basis Of Therapeutics, Ninth Edition, 1996, pgs. 1598-1605, previously submitted).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Ormerod et al. teach topical formulations, manufacture of a topical formulation and method for treatment of a dermatological condition comprising an immunosuppressive macrolide and a permeation modulator, which when applied to the skin produces a minimal systemic effect (see abstract). Specifically, the immunosuppressive macrolides taught include: sirolimus, FK-506 or SDZ ASM-981, which is also known as 33-epi-chloro-33-desoxyascomycin which conventionally are known to be applied by means of topical creams or taken orally (see pg. 1, lines 23-25, pg. 5, lines 3-4). In Example 3, topical sirolimus formulation applied to the skin of patients with chronic plaque psoriasis result in clinical improvement (see results found in Table 3, pg. 14). Additionally, Ormerod et al. teach that the formulation can be dissolved or suspended in any pharmaceutically acceptable carrier or vehicle such as water (see pg. 7, lines 26-28). Ormerod et al. also teach that systemic administration of macrolide immunosuppressants have been associated with undesirable side effects

when taken systemically for treating dermatological diseases, such as, psoriasis or atopic dermatitis (p. 3, lines 13-17); however, Ormerod et al. has overcome the problem by the formulation of topical macrolide immunosuppressants which reach the site of action via the incorporation of the permeation modulator.

Ormerod et al., however, does not teach the retinoid or the combination of macrolide immunosuppressive agents and retinoids.

Hardman et al. teach the utility of retinoids for effects on epithelia that have "revolutionized dermatological therapy in the last two decades" (see pg. 1598, section entitled, "Retinoids"). In Table 64-3, many retinoid- responsive skin diseases are listed and notably are acne, cutaneous aging and psoriasis (see p. 1599). Among the retinoids discussed are isotretinoin and etretinate (see p. 1599, Figure 64-2 and p. 1600-1602, sections entitled "Isotretinoin" or "Etretinate"). In addition to treatment using retinoids, Hardman et al. also teach that treatment of skin diseases, most notably--acne may also include additional therapeutic agents, such as, antibacterial agents which may be applied topically or given systemically (see pgs. 1604-1605). Thus Hardman et al. teach that retinoids and antibiotics are useful for treatment of dermatological diseases.

Because both Ormerod et al. and Hardman et al. teach the treatment of psoriasis using 33-epi-chloro-33-desoxyascomycin or retinoids, respectively; it is prima facie obvious to combine these two teachings with the result being that of the composition

and/or method of applicants' claims 1-3 and 6. The basis for this prima facie obviousness rejection can be found in the following case law: "It is however, prima facie obvious to combine two compositions taught in the prior art useful for the same purpose, in order to form a third composition to be used for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069,1072 (CCPA 1980).

Furthermore, one of ordinary skill in the art would have found it obvious to use the pharmaceutical composition described above either orally or topically for treatment of dermatological diseases as is suggested by Ormerod et al. and to further determine synergistic effective amounts. At the time of Applicants invention, it would have been obvious to one of ordinary skill in the art to make adjustments to the particular conventional working conditions (e.g., determining result effective amounts of the ingredients beneficially taught by the cited references), as well as treating a particular type of dermatological disease, is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan and no more than an effort to optimize results.

Applicants claim 4 drawn to a process of preparation of a composition according to mixing a macrolide and a retinoid with at least one pharmaceutically acceptable carrier is obvious to one of ordinary skill in the art as the end product may be made by many different processes which result in the same product. For example, a retinoid containing cream as described in Hardman et al. could be modified by mixing in the 33-

epi-chloro-33-desoxyascomycin resulting in a pharmaceutical composition of the instant claim.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ormerod et al. (WO 99/24036, previously submitted by applicant) in view of Hardman et al. (Goodman & Gilman's: The Pharmacological Basis Of Therapeutics, Ninth Edition, 1996, pgs. 1598-1605, previously submitted) as applied to claims 1-4, 6-7, and 9 above, and further in view of Remington's (The Science and Practice of Pharmacy, Nineteenth Edition, Vol I, 1985, pg. 806, previously submitted).

Ormerod et al. and Hardman et al. do not teach a kit comprising 33-epi-chloro-33-desoxyascomycin and retinoids with printed instructions.

Remington's: The Science and Practice of Pharmacy, Nineteenth Edition, Vol I, 1985, pg. 806 teaches that the inclusion of a package insert including "indications and use" of the pharmaceutical composition is mandated by 21 CFR 201.57.

At the time of Applicants' invention, it would have been obvious to one of ordinary skill in the art to include a label and packaging in the combined composition of Ormerod et al. and Hardman et al. One of ordinary skill in the art would have been motivated to include the packaging and the insert, because it is mandated by law as taught in Remington's.

Furthermore, It is well-settled law that combining printed instructions and an old product into a kit will not render the claimed invention nonobvious even if the instructions detail a new use for the product. See In re Ngai, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004). Further, the inclusion of a package insert or label showing the "the name of drug, dosage, dosage form, route of administration, indication and direction of use" of a pharmaceutical composition is mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art.

Claims 1-3 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaishnaw et al. (U.S. 2003/0185824 A1).

Vaishnaw et al. teach compositions and methods for treating or preventing an epidermal or dermal disorder including psoriasis and atopic dermatitis comprising a CD2-binding agent in combination with auxiliary agents and a pharmaceutical carrier (see abstract, pg. 8, paragraph 0105, and pg. 18, paragraphs 0204-0205). Exemplary auxiliary agents include retinoids such as etretinate and cytokine inhibitors such as pimecrolimus (i.e. 33-epichloro-33-desoxyascomycin) or any combinations thereof (see pgs. 2-3, paragraphs 0023-0024 and pg. 16, paragraphs 0187-0188). Importantly, Vaishnaw et al. teach the pharmaceutical composition can be administered systemically (i.e. intravenously, etc...), by infusion, orally or topically (see pg. 17, paragraphs 0194 and 0208).

Vaishnaw et al. do not teach compositions comprising exclusively 33-epi-chloro-33-desoxyascomycin and retinoids.

However, Vaishnaw et al. do teach that formulations can be made using 33-epi-chloro-33-desoxyascomycin or retinoids for the treatment of autoimmune disorders or chronic inflammatory disorder. Thus, it would have been obvious to one of ordinary skill in the art to combine both 33-epi-chloro- 33-desoxyascomycin and retinoids in the composition of Vaishnaw et al. as Vaishnaw et al. teach that each compound can be added to his composition for the treatment of psoriasis. Given the teachings of Vaishnaw et al., one of ordinary skill in the art would have been motivated to add both retinoids and 33-epi-chloro-33-desoxyascomycin to the composition of Vaishnaw et al. with the reasonable expectation of obtaining a composition that is highly efficacious in treating psoriasis.

Moreover, as a general principle it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining them flows logically from their having been individually taught in the prior art. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06.**

Regarding the claim limitation in claim 3 which requires the amount of 33-epi-chloro- 33-desoxyascomycin and retinoids to be additive or synergistic, it would have been obvious to a skilled artisan that the addition of both 33-epi-chloro-33-desoxyascomycin and retinoids would necessarily be either additive or synergistic given that Vaishnaw et al. teach their effective used in treating psoriasis. Thus, it would be well within the purview of the skilled artisan to optimize the different concentrations of the two drugs in order to determine the additive or synergistic effects of the two combined drugs.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

08/05/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617